Life Sciences Enterprise
DuPont Pharmaceuticals Company

November 1, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Ladies and Gentlemen:

Ref: Docket Number 99D-2729 (CDER 98161)

We are writing to provide comments concerning the following Guidance for Industry: "BA and BE Studies for Orally Administered Drug Products – General Considerations".

DuPont Pharmaceuticals Company wishes to provide its endorsement of the above proposed guidance's recommendation that bioequivalence studies between the reference drug and generic drug products use more stringent criteria in establishing bioequivalence when those drugs are narrow therapeutic range drugs (Section V.C.1.). As noted in section V.F., some FDA and USP documents currently recommend additional testing and/or controls to ensure the quality of drug products containing narrow therapeutic range drugs. Specifically, the use of a 90 – 111% limit rather than the 80-125% limit currently used will help insure any differences between these narrow therapeutic range products are not clinically significant. We also are in agreement that the examples of narrow therapeutic range drugs specifically include all warfarin products.

The inadequate evaluation of bioequivalence with narrow therapeutic range generic drugs constitutes a dangerous potential safety issue; the recommendations of this guidance related to increased stringency for bioequivalence determination in the case of narrow therapeutic range drugs are a valuable and necessary change to the current system of ANDA approval. By requiring more stringent bioequivalence criteria, an increased assurance of interchangeability for drug products containing the specified narrow therapeutic range drugs should be achieved.

Sincerely,

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